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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/826,788	04/16/2004	Fabrice Chimienti	20349-564	1282

30623 7590 01/06/2006

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EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 01/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/826,788	CHIMIENTI ET AL.	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-12 and 60* is/are pending in the application.

4a) Of the above claim(s) *8 and 13-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 9-12, and 60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8/25/04, 11/16/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I, claims 1-7, 9-12, and 60, drawn to a method for treating a neurological disorder in a subject by administering an effective amount of SLURP-1 protein in the reply filed on 17 October 2005 is acknowledged. Because Applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP §818.03(a)).

2. Claims 8, 13-59 and 61-79 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 17 July 2005.

3. The restriction requirement is still deemed proper and is therefore made FINAL.

Status of Application, Amendments, and/or Claims

4. The response to the second restriction requirement filed 17 October 2005 has been received and entered in full. Claims 8, 13-59 and 61-79 have been withdrawn from further consideration as discussed above. The Examiner recognizes Applicant's right to pursue additional subject matter in other applications. Therefore, claims 1-79 are pending and claims 1-7, 9-12, and 60 are the subject of this Office Action. The claims also read upon the following species: schizophrenia disease from the neurological disorder group.

Information Disclosure Statement

5. The information disclosure statements (IDS) filed 16 November 2004 and 25 August 2005 have been considered by the examiner.

Specification

6. The disclosure is objected to because of the following informalities:

7. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Appropriate correction is suggested.

Claim Objections

8. Claims 5 and 60 are objected to because of the following informalities: (a) Claim 5 encompasses non-elected inventions, e.g., pain, neuropathic pain, cognitive impairments, Alzheimer's disease, and Parkinson's disease. (b) Claim 60 depends from claim 58, which is currently withdrawn.

Appropriate correction is suggested.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-7, 9-12, and 60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

11. Claims 1-7, 9-12, and 60 are directed to a method for treating a neurological disorder in a subject comprising administering an effective amount of SLURP-1 protein. The claims also read upon the following species: Alzheimer's disease from the neurological disorder group. However, the instant specification fails to teach how to achieve the proposed treatment, thus requiring undue experimentation of one skilled in the art to use the claimed invention with a reasonable expectation of success.

12. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

13. The Specification discloses a SLURP-1 polypeptide set forth as SEQ ID NO:2. The Specification also teaches that SLURP-1 protein of SEQ ID NO:2 modulates the activity of the alpha7 nicotinic acetylcholine receptor (See pg 6, lines 11-21; Figures 5A-5C). The Specification also teaches that signaling through the alpha7 nicotinic acetylcholine receptor is essential for epidermal homeostasis and plays an essential role in inflammation (See pg 7, lines 14-30), a finding which is supported by the teachings of the art (See for example Arredondo et

al. (2002). "Central role of alpha7 nicotinic receptor in differentiation of the stratified epithelium". The Journal of Cell Biology. 159(2):325-336; Wang et al. (2003). "Nicotinic acetylcholine receptor alpha7 subunit is an essential regulator of inflammation". Nature. 421:384-388, cited by Applicant). Accordingly, the Specification teaches that SLURP-1 is useful in the treatment and/or prevention of a pathology caused by dysfunction of an acetylcholine receptor, including neurological disorders such as pain, neuropathic pain, schizophrenia, cognitive impairments, Alzheimer's disease, and Parkinson's disease, as well as skin pathologies such as Mal de Meleda, wound healing, and psoriasis (See pg 3, lines 24-28). Therefore, although it has been established that the alpha7 nicotinic acetylcholine receptor is an important mediator in epidermal homeostasis and inflammation, and that mutations in SLURP-1, a compound which has been demonstrated to modulate the activity of the alpha7 nicotinic acetylcholine receptor in vitro, have been implicated in Mal de Meleda, there is no nexus between the SLURP-1 protein and any "neurological disorder" which is to be treated, Therefore, one skilled in the art would not expect that administration of SLURP-1 would result in treatment of Schizophrenia or any "neurological disorder". One skilled in the art would not know, with any level of predictability, that the administration of an undetermined amount of SLURP-1 protein would lead to the treatment of schizophrenia or any "neurological disorder".

14. The instant specification does not teach how to treat schizophrenia or any "neurological disorder. The specification fails to disclose how to assess *in vivo* a pharmaceutically effective amount of SLURP-1 protein, nor has it established a nexus between the SLURP-1 and any "neurological disorder" which is to be treated. Moreover, the specification fails to disclose whether or not the SLURP-1 protein that is administered would cross the blood brain barrier and

reach the target cells at a concentration sufficient for treatment, which is a major obstacle for this type of therapy (See Miller, G. "Breaking down barriers". Science 297:1116-1118, 2002). The art also teaches that the goal of delivering proteins and peptides noninvasively has only achieved modest success, with poor applicability to proteins and peptides (See for example Pettit et al. "The development of site-specific drug-delivery systems for protein and peptide biopharmaceuticals". Trends Biotechnol. 16: 343-349, 1998; See especially pg 343, col 1-2). The problems posed by proteins and peptides are their large molecular size, electrical charge, relatively hydrophilic nature, and relative instability in environments of extreme pH or proteolytic activity (such as the stomach and intestine) (pg 343, col 2). Pettit et al. review several routes of protein administration and the limitations that have been encountered. For example, limited success has been achieved delivering proteins and peptides orally because of: 1) poor intrinsic permeability across intestinal epithelium, 2) susceptibility to enzymatic attack, 3) rapid post-absorptive clearance, and 4) chemical instability (pg 344-345). Although much effort has been given to the transdermal delivery of pharmaceutical products, clinical applications have been limited to non-protein drugs because of the skin's poor permeability to proteins and peptides (pg 343, col 2). Additionally, proteins or peptides administered systemically must resist clearance via molecular filtration by the kidney and clearance by the reticuloendothelial system (pg 345, col 2). Therefore, the state of the prior art establishes the unpredictability of delivering proteins to a subject, particularly those targeting the brain. In the absence of this guidance, a practitioner would have to resort to a substantial amount of undue experimentation involving the variation in the amount and duration of administration of SLURP-1 protein, and making a determination of whether a successful result was achieved. The instant situation is directly

analogous to that which was addresses in *In re Colianni*, 195 USPQ 150, (CCPA 1977), which held that:

> "a "[d]isclosure that calls for application of "sufficient" ultrasonic energy to practice claimed method of fusing bones but does not disclose what "sufficient" dosage of ultrasonic energy might be or how those skilled in the art might select appropriate intensity, frequency, and duration, and contains no specific examples or embodiment by way of illustration of how claimed method is to be practiced does not meet requirements of 35 U.S.C. 112 first paragraph".

15. There are no working examples presented in the instant specification that describe the successful treatment of schizophrenia or any other neurological disorder with the SLURP-1 protein of the instant invention. Therefore, even if, *arguendo*, a nexus between the SLURP-1 polypeptide and the pathogenesis of schizophrenia were established, one skilled in the art would have to perform an undue amount of experimentation to use the claimed methods to treat schizophrenia or any "neurological disorder".

16. Thus, in view of the lack of teachings and unpredictability of the art set forth above and the total absence of working examples, the instant specification is not found to be enabling for a method for treating schizophrenia or any other neurological disorder by administering an effective amount of SLURP-1 protein to the subject. It would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to use the Applicants' invention as currently claimed.

Claim Rejections - 35 USC § 112, 2nd Paragraph

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 1-7, 9-12, and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

19. Claims 1-7, 9-12, and 60 are rejected as being indefinite because the mere recitation of a name, i.e. SLURP-1, to describe the claimed invention is not sufficient to satisfy the statutes requirement of adequately describing and setting forth the inventive concept. In order to avoid possible confusion over proteins with the same or similar names that may be found to have patentably different structure and/or utility, proteins claimed by a particular name should be further distinguished in the claims by conventional protein characterization according to known parameters, e.g. such as by molecular weight, pI, *amino acid sequence information*, whether the protein is a monomer or multimeric, function(s) and/or activity, and/or other finger-printing techniques such as IR, NMR, or UV spectroscopy data and/or other known properties which would serve to distinguish the claimed protein from other proteins. In addition, in consideration of the discrepancies often encountered in the art between protein molecular weights when determined by different methods, whenever a molecular weight is recited to characterize a protein the claim should include the method by which it was determined, e.g. whether by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE), gel filtration or some other method, and whether reducing or non-reducing (native) conditions were used.

20. Claims 1-7, 9-12, and 60 are rejected as being indefinite because the claims do not have a step that clearly relates back to the preamble. For example, there is no step indicating that administration of SLURP-1 results in treatment of a neurological disorder, nor is there guidance as to the desired outcome.

21. No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JML
January 4, 2006

Bridget E. Bunner

BRIDGET BUNNER
PATENT EXAMINER